Preliminary and Short Report

ELECTRON MICROSCOPY OF VIRUS-LIKE PARTICLES IN A KERATOACANTHOMA*

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In recent years numerous papers have given detailed descriptions of the gross and microscopic structure of keratoacanthomas (1-6). Briefly, localized keratoacanthomas are usually single and on exposed areas, grow rapidly and regress spontaneously. The keratoacanthoma begins as a papule, sharply delimited from the surrounding tissue, increases in size to become warty and dome-shaped with a central keratin-filled crater. The histopathologic picture resembles a low grade squamous cell carcinoma and differentiation is at times impossible without the help of the clinical pattern. Although authors believe that the localized or solitary type of keratoacanthoma is related to the multiple type there is no general consensus.

A variety of agents have been indicted as possible causes of keratoacanthoma: so varied as sunlight, trauma, genetic factors, nevoid origin, virus infection, aging, contact with oils and tars, changes in sebaceous cysts and occlusion of the pilosebaceous apparatus. Several observers have suggested that a virus might be the etiologic agent. Dibden and Fowler (7) reported multiple keratoacanthomas occurring in a donor site following surgical removal of several keratoacanthomas from the dorsal surface of the hand. A similar observation has been reported by Brown and Fryer (8). Ereaux and co-workers (9) with the use of culture methods and metal shadowing technics, were able to isolate virus-like particles from one keratoacanthoma. Also suggestive of a viral cause is its rapid growth and spontaneous disappearance as well as its warty appearance.

In the past several years technical advances in the field of electron microscopy have also progressed rapidly. The development of adequate methods for thin sectioning has led to increased data regarding structure and intracellular behavior of tumor viruses. At present, though, such information is still incomplete. Bernhard (10) has recently reviewed this subject in detail. In general, viruses range in size from 10 mμ to 300 mμ. As regards shape, tumor viruses as seen in thin sections are round to oval. The virus consists of a central dense nucleoid which is surrounded by one or more lipoprotein membranes. The nucleoid is supposed to be composed of nucleoprotein and to carry the infective particle. Viruses have been noted either in the nucleus or the cytoplasm or in both the nucleus and the cytoplasm.

The purpose of this study was to evaluate the ultrastructure of the keratoacanthoma using the newer technics in electron microscopy with particular reference to virus particles.

MATERIALS AND METHODS

The tumor studied was a typical keratoacanthoma removed from the forehead of a 57 year old man. The growth was excised and bisected. One half was immediately fixed in buffered 1% osmium tetroxide and embedded in Vestopal W in a manner previously described (11). The thin sections were stained with uranyl acetate for two hours prior to being studied with an RCA EMU-3F electron microscope. The second half was fixed in formalin and stained with hematoxylin and eosin. The microscopic sections stained with hematoxylin and eosin were characteristic for a keratoacanthoma. The general histopathologic structure of such tumors has been previously described thoroughly.

RESULTS

Many virus-like particles are consistently noted within the nuclei of cells making up the keratoacanthoma (Figs. 1 & 2). Such structures are not seen in the surrounding stroma nor in any other cells except those of the tumor. These virus-like particles are found in all regions of the growth and in 40-60% of the tumor cells seen in each section. There are from one to seven particles within each "infected" nucleus in any one section. The par-

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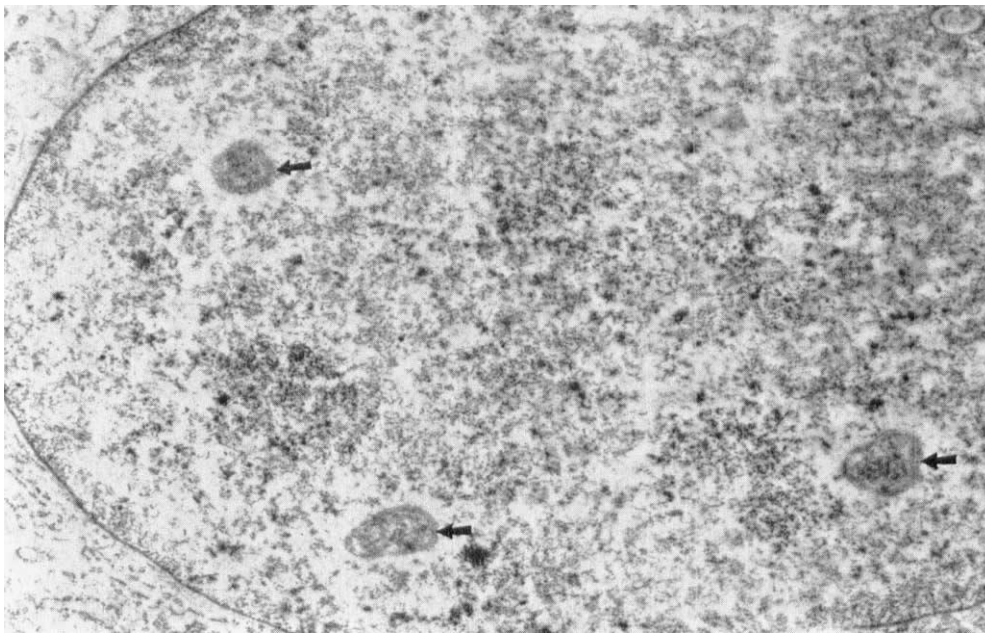

FIG. 1. Three virus-like particles are shown within the nucleus. × 16,200

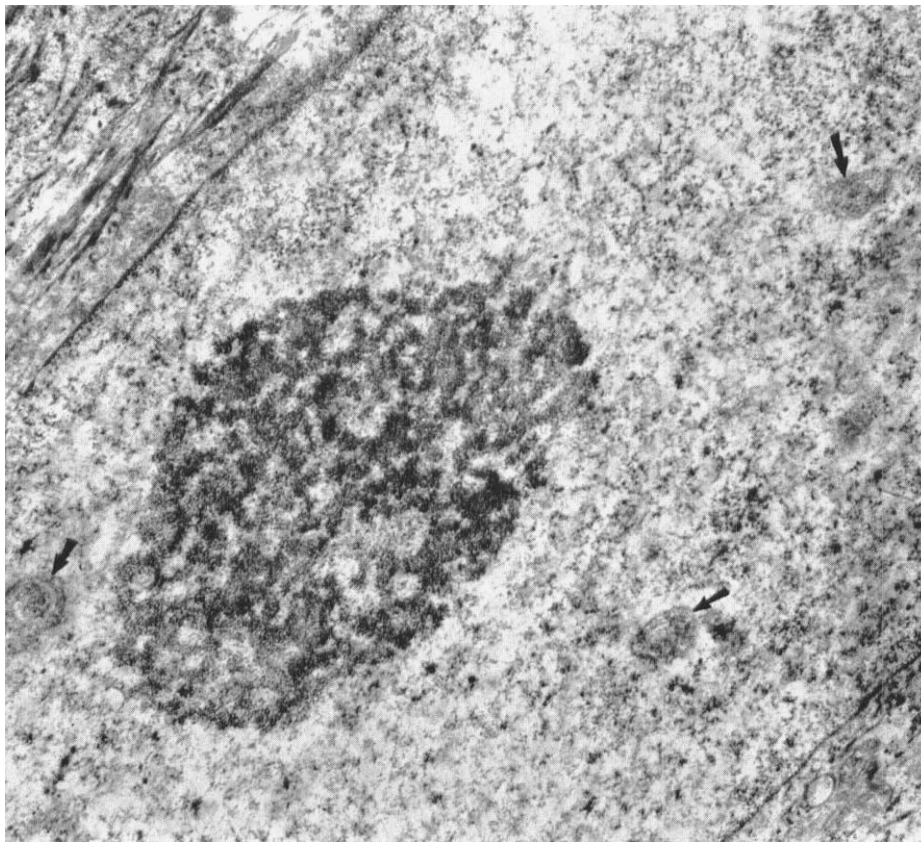

FIG. 2. A nucleus containing a large granular nucleolus as well as three virus-like particles. × 16,200

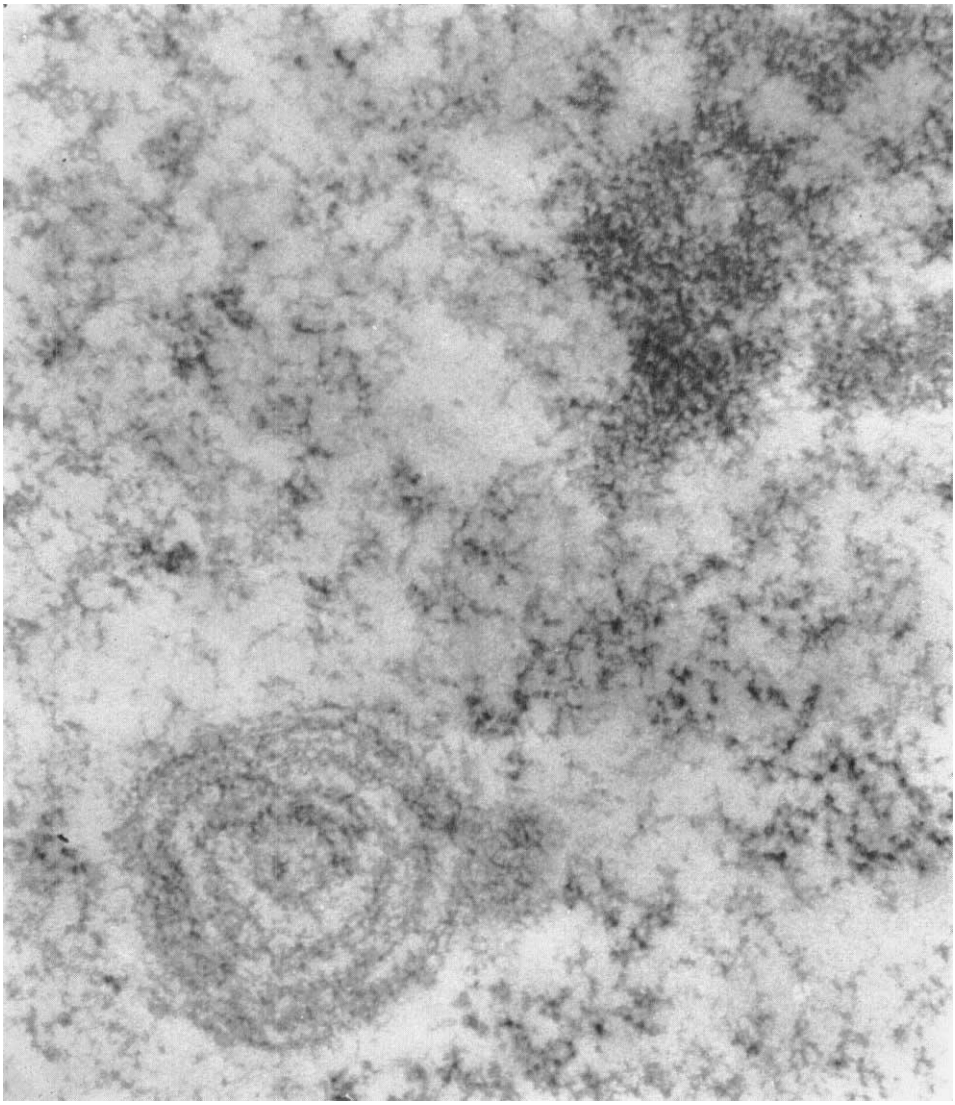

FIG. 3. The typical virus-like particle has a small central nucleoid and is surrounded by four membranes. Each membrane is composed of two osmiophilic layers separated by a constant less-dense region. A portion of the nucleolus is located in the upper right corner. × 82,763.

ticles are located in the nucleoplasm between the nucleolus and the nuclear membrane and the involved nuclei and nucleoli are markedly increased in size and granularity.

When seen in thin sections the virus-like particles (250–600 mμ) are round or oval. They consist of a central nucleoid (20–40 mμ) which is surrounded by a spiral array of two to five membranes. With higher magnification each membrane is noted to consist of two dense layers separated by a distance of 18 mμ. Each bilamellar membrane is separated from its neighbor by 40 mμ (Fig. 3). There is one clear zone or halo surrounding the nucleoid and another surrounding the virus-like particle as a whole. On rare occasions the nucleoid may measure 125 mμ in diameter and in these cases the surrounding membranes are not distinct (Fig. 4).

DISCUSSION

The keratoacanthoma studied was untreated prior to its excision; therefore any alterations noted were not iatrogenic. Virus-like particles were present in all regions of the tumor and in

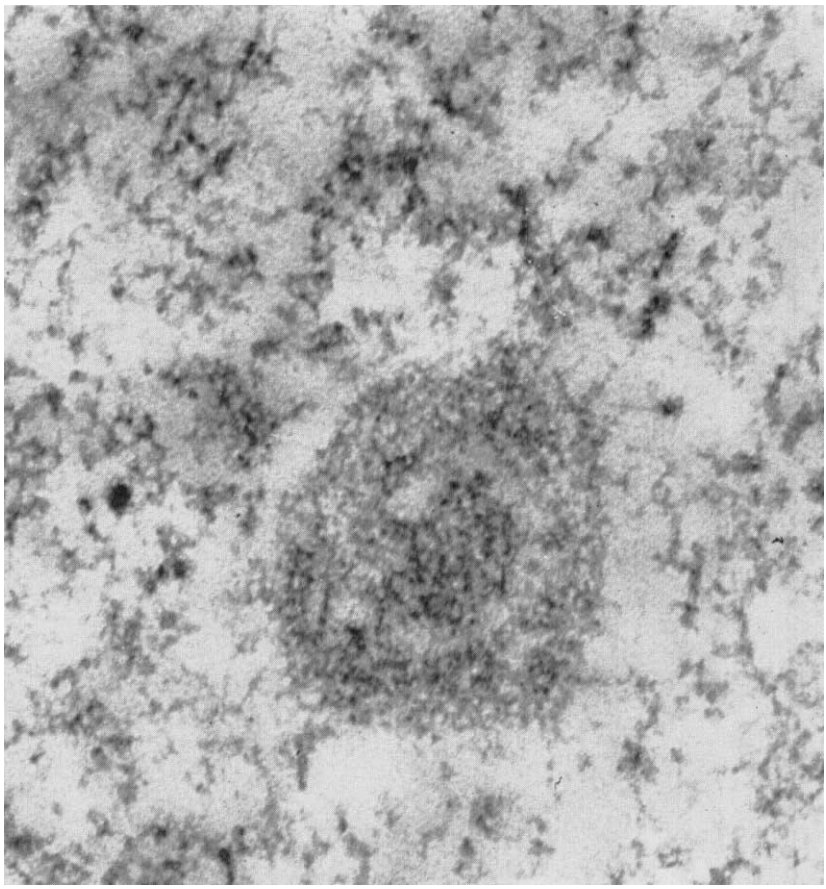

FIG. 4. A virus-like particle located within a nucleus. In this section the "nucleoid" is large and the surrounding membranes are not distinct. × 117,750.

large numbers within the tumor thus making it likely that they are of a specific nature rather than a non-specific change. In thin sections the particles are slightly larger than the average size given for viruses. It remains to be seen whether this structure is definitely viral, and if so whether it plays a role in the etiology of keratoacanthoma. At present all that can be said is that the alteration is present in many cells of this particular tumor, consistently occurs within the nucleus, is of a constant size, is apparently specific for the keratoacanthoma and that it has a virus-like structure.

SUMMARY

Virus-like particles have been demonstrated in a keratoacanthoma by means of electron microscopy. These particles are found in 40–60% of the tumor cells and are located within the nucleus. The composition of these particles has been deribed and their significance pointed out.

ADDENDUM

Since submitting this manuscript for publication we have had an opportunity to study three more keratoacanthomas. Similar virus-like particles, located within the nuclei, were found in all three tumors, however, in two of these tumors the particles were present in only 15–25% of the cells

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